Tenofovir and Emtricitabine in the Monotherapy for Hepatitis B

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Tenofovir disoproxil fumarate (TDF) is a nucleotide analog and a congender of adefovir dipivoxil (ADV). The 300 mg dose is licensed for the treatment of HIV-1. However, it has been shown to have *in vitro* activity against both wild-type and 3TC-resistant HBV.[1,2] There are no randomized controlled trials of TDF in HBV infection. There are case series showing the activity of TDF in mono-infected and co-infected HBV patients.[3,4] The HBV YMDD mutant that is resistant to 3TC is sensitive to ADV and TDF both *in vivo* and *in vitro*.[5-7] TDF has been used to rescue patients with end-stage liver disease in ADV resistant HBV[8] and after liver transplantation.[9] Van Bommel, et al. compared ADV and TDF in a case series of 53 patients with active viral replication (HBV DNA >6 log10 copies/mL) and genotypic evidence of lamivudine resistance.[3] Thirty-five patients received TDF for 72 to 130 weeks, and 18 received ADV for 60 to 80 weeks. Although not randomized, early viral kinetics revealed that TDF-treated patients showed a strong and early suppression of HBV DNA compared to ADV within a few weeks, whether they were HBV mono-infected or co-infected with HIV. After 48 weeks of therapy, 44% of patients receiving ADV had HBV DNA levels below 10^5 copies/mL in contrast to 100% of those receiving TDF. Resistance is rare, and the clinical implications of genotypic resistance are not yet clear.

Emtricitabine (FTC) is a cytosine nucleoside analog approved for treatment of HIV infection. A randomized placebo controlled study of 167 HBV patients showed improved histology in those receiving FTC, both in patients with chronic hepatitis Be (HBe) antigen positive and negative disease. Fifty-four percent of patients receiving 200 mg FTC had serum HBV DNA less than 400 copies/mL at week 48 compared to 2% of controls.[10] Subjects had biochemical, histologic, and virologic responses compared to placebo. YMDD mutations were detected in 19 patients with detectable virus at week 48. Post treatment exacerbation of HBV infection developed in 23% of emtricitabine-treated patients.[11]

Both TDF and FTC have long half lives and require once daily dosing. Because of predominantly renal excretion, they must be dose adjusted in cases of renal insufficiency. A combination of both drugs is in use for HIV therapy with 300 mg TDF and 200 mg FTC.

Randomized controlled studies of TDF and dose ranging studies for HBV have not been performed. Whether combination therapy with FTC and TDF will be of value in HBV infection to improve efficacy and decrease resistance has not been studied as yet.

References

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